

Claim Amendments:

51. (New) A composition for detecting the effect of an enzyme on a peptide substrate, the activity of said enzyme being effective to convert said peptide substrate ,w/o cleavage, from an unmodified state to a modified state, said composition comprising a functional peptide substrate for said enzyme, having a first detectable proximity-sensor peptide incorporated into a first position of said substrate and a second detectable proximity-sensor peptide incorporated into a second position of said substrate, thereby providing a semi-synthetic multiple labeled polypeptide substrate having a first structural conformation in said unmodified state and a second structural conformation in said modified state, said proximity sensors being spaced apart in said first structural conformation at a distance which is characteristic of said unmodified state and being spaced apart in said second structural conformation at a distance which is characteristic of said modified state, detection of one of said structural conformations being indicative of the effect of said enzyme on said substrate.

52. (New) The composition of claim 51, wherein said enzyme is a kinase.

53. (New) The composition of claim 52, wherein said kinase is Abelson protein tyrosine kinase.

54. (New) The composition of claim 51, wherein said peptide substrate is Crk-II.

55. (New) The composition of claim 51, wherein said modification of said substrate is a post-translational type modification.

56. (New) The composition of claim 55, wherein said modification of said substrate is a phosphorylation modification.

57. (New) The composition of claim 55, wherein said modification of said substrate is a dephosphorylation modification.

58. (New) The composition of claim 51, further comprising a modulator of said enzyme.

59. (New) The composition of claim 58, wherein said modulator of said enzyme inhibits said enzyme activity.

60. (New) The composition of claim 58, wherein said modulator of said enzyme activates said enzyme activity.

61. (New) The composition of claim 51 wherein said first detectable proximity-sensor peptide is at the N-terminus, the C-terminus of which is peptide-bonded to the N-terminus of said semi-synthetic multiple labeled polypeptide, the C-terminus of which is peptide bonded to the N-terminus of said second detectable proximity-sensor peptide.

62. (New) The composition of claim 51 wherein said peptide substrate is a recombinant polypeptide.

63. (New) The composition of claim 51 wherein said first and second detectable proximity-sensor peptides of said semi-synthetic multiple labeled polypeptide comprise a FRET pair.

64. (New) The composition of claim 63 wherein said FRET pair is selected from the group consisting of fluorescein and tetramethylrhodamine, IAEDANS and fluorescein, EDANS and DABCYL, BODIPY fluorescein and BODIPY FL fluorescein, β -phycoerythrin and CY5, and pyrene and coumarin.

65. (New) The composition of claim 63, wherein said FRET pair comprises fluorescein and tetramethylrhodamine.

66. (New) The composition of claim 51 wherein said detectable proximity-sensor peptide is a synthetic oligopeptide comprising a fluorescent amino acid derivative.

67. (New) The composition of claim 51 as set forth in Figure 5A (SEQ ID NO: 8).

68. (New) The composition as shown in SEQ ID NO: 9.